SOP number	**51.016**	Version	**6.0**
Title	**Preparation and Maintenance of a Trial Master File**		

Prepared by Signature	Louise Ner Date
Approved by Signature	Melissa Robert Date
Released by Signature	Jesse Dawson Date

SOP category	NHS GG&C Sponsor R&I

Staff category

Staff Category	R	A	C	I
Research & Development Systems Manager		X		
Research Governance	X			
Sponsor Research Co-ordinator	X			
Senior Research Administrators	X			
R&I Sponsor Pharmacy	X			
Project Management	X			
Contract Manager	X			
Industry Collaboration Project Manager	X			
University of Glasgow Head of Research Regulation and Compliance			X	
Data Management				X
Chief Investigator				X
Laboratories (Involved in Primary and Secondary End Points)				X

1. Scope

This procedure applies to Clinical Trial Investigational Medicinal Products (CTIMPs) and Clinical Investigations of Medical Devices (CIMDs) sponsored by NHS Greater Glasgow Health Board (NHSGGC), or co-sponsored with University of Glasgow (UoG). The conduct of a trial must be able to be reconstructed both during the trial and for some time after its completion from the documentation which is filed and retained within the trial master file (TMF).

2. Purpose

This procedure applies to NHSGGC R&I Department and details the process for preparation and maintenance of a TMF. A TMF is the collection of documentation that allows the evaluation of the conduct of the CTIMP/CIMD, the integrity of the trial data and the compliance of the trial with Good Clinical Practice (GCP).

3. Procedures

3.1. Abbreviations/Definitions

CIMD	Clinical Investigation of a Medical Device
CTIMP	Clinical Trial of an Investigational Medicinal Product
GCP	Good Clinical Practice
CI	Chief Investigator
PI	Principal Investigator
PM	Project Manager
R&I	Research & Innovation department
RC	Sponsor Research Co-ordinator
SRA	Senior Research Administrator
RCB	Robertson Centre for Biostatistics
TMF	Trial Master File
ISF	Investigator Site File
UoG	University of Glasgow
SIV	Site Initiation Visit
Essential documents	individually or collectively permit evaluation of the conduct of a trial and the quality of the data produced

3.2. TMF Overview

The TMF contains all trial essential documentation which should be sufficient to adequately reconstruct the trial activities undertaken, along with key decisions made concerning the trial. The complete TMF includes the Sponsor/Co-Sponsor TMF, Investigator Site File (ISF) as well as participant medical records.

R&I NHSGGC Sponsor/Co-Sponsor team includes a number of sub departments/teams and representatives from these teams form the overall Sponsor/Co-Sponsor team assigned for individual CTIMP/CIMD oversight. All teams will follow this SOP and prepare their designated section of the complete TMF index (Form 51.016A) independently, after being notified that a Sponsored CTIMP/CIMD funding application has been successful.

For international trials where NHSGGC are acting as Lead Co-ordinating Centre for the UK, the RC will liaise with Sponsor after a successful application to determine what files (if any) will be retained by NHSGCC and how long for. Arrangements for these files will be detailed in the contract with the Sponsor and disseminated to all relevant teams and/or third parties.

3.3. TMF Preparation and Maintenance

3.3.1. Sponsor/Co-Sponsor Trial Master File (TMF)

The Sponsor/Co-Sponsor TMF index is divided in sections and covers the following teams and third parties:

A. R&I Sponsor Systems/Innovation (Sections 1-9)
B. Pharmacy (Section 10)
C. Pharmacovigilance (Section 11)
D. Monitoring (Section 12)
E. Governance (Section 13)
F. Project Management (Section 14)
G. Data Management (Section 15)
H. Vendors (i.e. Laboratories) (Section 16)

All required documents, as per the complete TMF index (Form 51.016A), will be printed to comprise a paper TMF and stored in a locked cabinet in the corresponding team office. These documents will be added to each team's file once available (or at minimum every 6 months) and a copy of each document will be saved electronically in the trial e-folder, however the e-folder will not be considered the TMF. As there is not currently a validated system in place to act as an electronic TMF, all documents must be printed and filed as standard. If a section of the TMF is to be stored electronically this must be validated and approved by the owner of that section. Failure to print and maintain the TMF as per this SOP will constitute a Non-Compliance.

Sections of the TMF will be maintained by the appropriate individuals of the relevant team for the whole length of the trial until archived according to SOP 51.024. All study documents must be filed in sequential order with the most recent on top. It is essential to maintain the file with up to date information, anything not filed within the paper TMF section will be considered missing information, even if present on common drives or in personal folders. Only the printed and filed documents will comprise the TMF unless otherwise stated within the paper TMF.

Sponsor/Co-Sponsor email correspondence detailing decision making will be filed in the appropriate sections of the TMF and a copy will be stored electronically in the trial e-folder. All other relevant Sponsor/Co-Sponsor email correspondence will also be stored electronically in the trial e-folder and on the corresponding department/institution's server.

The individual(s) responsible for the TMF section will assume responsibility for maintenance throughout the lifetime of the study (unless otherwise delegated). If other individuals wish to add/ amend/ remove a document from the TMF, they must make the responsible individual(s) aware.

A. R&I Sponsor Systems/Innovation (Sections 1-9)

The SRA will be responsible for creating the R&I Sponsor Research Co-ordinator TMF file (Sections 1-9) after MHRA approval of a trial and maintaining the file for the duration of a trial. The RC will be responsible for QA checks at minimum every 6 months and prior to archiving. The R&I Sponsor Research Co-ordinator File will contain the cover sheet (Form 51.016J) indicating the storage locations, format and point of contact for all wider Sponsor/Co-Sponsor team files as well as third party vendor files.

F. Project Management (Section 14)
Project Managers (PMs) or their designees working across Glasgow Oncology Clinical Trials Unit (GO CTU) coordinating CTIMPs and CIMDs will maintain components of the TMF as per this SOP and GO CTU SOPs.

All other PMs including those in the Project Management Unit (PMU), the University of Glasgow (UoG), Robertson Centre for Biostatistics (RCB), the Innovation team as well as external PMs coordinating CTIMPs and CIMDs will maintain the relevant components of the TMF following this SOP.

G. Data Management (Section 15)
Data Management centres including RCB and other third party data processors will be responsible for preparing, maintaining and archiving their corresponding section of the TMF.

H. Vendors (e.g. Laboratories) (Section 16)
If the CTIMP/CIMD involves the use of a vendor (e.g. laboratories for sample processing and analysis), it will be expected that the vendor will maintain and store documents that they are responsible for and will make them available for audit/inspection as required. Storage and maintenance of trial documents will be clearly documented in the appropriate contracts. This will be prepared by the RC liaising with the Vendor.

The Sponsor/Co-Sponsor will provide vendors with a TMF plan, as recommended by the MHRA, that cover the following points:

- Who holds the official TMF (or which parts each party holds when this is divided)
- The process of filing documentation in the TMF
- Documents that both parties must retain
- The structure of indexing of the TMF
- When eTMF is used - details of the system
- Access arrangements in place for both parties for oversight and trial management
- How TMF would be available if either party was inspected
- Arrangements for when the trial is completed - Archiving

The vendor TMF plan will be included in the contractual arrangement between the Sponsor/Co-Sponsors and the vendor involved in the trial and will be captured on Form 51.016L. Section 16 will be required for all Vendors used within the trial, regardless of whether or not they have undergone a vendor assessment in accordance to SOP 51.015.

Guidance on completing the TMF sections is available in Guideline 51.016B.

3.3.2. Investigator Site File (ISF)

The ISF file is prepared by the PMs using Form 51.016C and sent to each participating site as per SOP 56.001. Participating sites will be responsible for preparing, maintaining and archiving their corresponding part of the TMF (in the form of the ISF) independently of one another according to their local processes and/or as per Sponsor/Co-sponsor instructions or agreed terms within the mNCA and this SOP.

The source data plan (Form 56.002M) will cover information on the local flag system for medical records of the participants in the trial. This will also be discussed prior to/at the Site Initiation Visit in order to ensure that the participants' medical records will be retained for the duration of archiving period of the trial as well as according to the local policies.

3.4. File Notes

On occasion it may be required to add a file note to the TMF to explain a particular course of action taken during the trial or clarify the information present for future observers. Form 51.016M may be used to document this information. Other organisations involved in the running of the trial may have their own format for file notes which may be used, for activity relating to that which NHSGGC R&I are responsible for, Form 51.016M should be used and signed by R&I staff. A file note cannot be used in place of Non-Compliances or SOP waivers and are simply there to document and explain events that have taken place for ease of understanding the TMF documentation at a later date.

3.5. Quality Control (QC)

All sections of the TMF will be subject to QC review at least once in the lifetime of the of a trial: during set-up, conduct, close-out/reporting and before archiving. However, the contents of the TMF should be QC'd on an ongoing basis as the documents are filed or at minimum, every 6 months. The QC review will involve the reviewer (the corresponding representative of each Sponsor/Co-Sponsor team) ascertaining that the TMF contents match the TMF index requirements and that the locations of documents is correct according to the index and any other directions provided. The review will be captured by each team in the corresponding cover page in Form 51.016K and any inconsistencies/ errors/ omissions will be actioned to correct the issue.

Once addressed, the person performing QC will add their name and the date in the "Signature/Date" part of the corresponding QC section. Actions must then be taken, where possible, to remove any issues identified within the TMF. Individual TMF Files may also be subject to QC review and audit by a designated member of the Research Governance team. When a review by the Governance Team has been completed, this will be documented by an audit and an audit report will be provided to the individual responsible and they will correct any inconstancies/ errors/ omissions in a timely fashion.

3.6. Archiving of TMF

The TMF will be archived according to SOP 51.024.

4. Referenced documents

- Form 51.016A - Complete R&I TMF Index
- Form 51.016C - Principal Investigator Site File: Essential clinical trial documentation for academic (non-commercial) trials
- From 51.016J - TMF Cover Sheet
- Form 51.016K - TMF index pages
- Form 51.016L - Vendor TMF Plan Template
- Form 51.016M - TMF/ISF File Note
- SOP 51.015 – Assessment of Vendors
- SOP 51.024 - Archiving Essential Documents from Clinical Research – Process for a Sponsored Clinical Trial of an Investigational Medicinal Product (CTIMP)
- SOP 56.001 - Site Set Up – Green for Go Process
- Form 56.002M - Source Data Plan
- GUI 51.016A - Quality Control of Trial Master File
- GUI 51.016B - Sponsor TMF Index Guidelines
- https://tmfrefmodel.com/ (CDISC – Trial Master File Reference Model)

5. Related documents

- None

6. Document history

Version	Date	Description
1.0	06/11/2013	Release of first version
2.0	14/07/2016	Updated to template v1.4 and to reflect inspection outcomes.
3.0	17/12/2018	Staff category, Author and Approver updated
4.0	04/10/2021	Author updated. Reference to two of the associated forms updated (CI site file – form 51.016B now CI file and Sponsor file now TMF index – 51.016A). Admin updates (job titles and R&I office name change included). Section 6 updated to reflect current SOP numbering. Version updated.
5.0	24/07/2023	Author updated. Significant text change to clarify the procedures covered. Creation of Forms K & L along with Removal of Forms B, D, E, F, G, H & I. Creation of Guideline 51.016A.
6.0	08/05/2025	Restructured info for clarity, updated CRUK CTU to GO CTU and further information on Vendors and file notes.